



GE Healthcare

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November 25, 2008

Carolyn Clancy, MD
Director
Agency for Healthcare Research and Quality
540 Gaither Road
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Re: Report to AHRQ from the Cancer Intervention and Surveillance Modeling Network (CISNET) for MISCAN, SimCRC, and CRC-SPIN Models - Project ID: CTCC0608, November 4, 2008

Dear Dr. Clancy:

GE Healthcare (GEHC) appreciates this opportunity to comment on the draft Report to AHRQ from the Cancer Intervention and Surveillance Modeling Network (CISNET) for MISCAN, SimCRC, and CRC-SPIN Models, November 4, 2008.

GEHC, a \$17 billion unit of General Electric Company that is headquartered in the United Kingdom, has expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, performance improvement, drug discovery, and biopharmaceuticals manufacturing technologies. GEHC's broad range of products and services enables healthcare providers to offer patients earlier and better diagnosis and treatment of cancer, heart disease, neurological diseases, and other conditions that threaten the quality and length of life. Worldwide, GEHC employs more than 46,000 people committed to serving healthcare professionals and their patients in more than 100 countries.

We applaud AHRQ for preparing a thorough and comprehensive analysis of CT Colonography (CTC). The report is well structured and organized, its purpose is clear, and its scope is well defined. The report confirms that CTC is a highly cost-effective solution for colorectal screening, which is already reflected in CTC screening being covered by many private payors, and reinforced by the recent favorable report issued by the BlueCross BlueShield Technology Evaluation Center¹.

When correctly characterized, the cost-effectiveness analyses in the AHRQ report conclude that CTC is a highly cost-effective addition to Medicare's colorectal screening benefit, and would be shown as an even better value to Medicare if certain technical corrections noted in our comments to the report were made.

We emphasize that CTC should be evaluated as another effective screening tool to improve CRC screening adherence, not as a substitute for existing CRC screening methods.

Overview of Comments

- **CTC should be assessed as an additional screening tool** - The analyses incorrectly presume that patients will switch from current screening options to CTC, not that CTC will result in more beneficiaries being screened for CRC. However, evidence and common sense suggest that CTC will

increase the number of beneficiaries screened because patients prefer non-invasive tests. Because CTC will likely increase screening adherence, it should be evaluated by comparing Medicare's current screening *program* (stool testing or endoscopic examinations) to probable Medicare screening *program scenarios* that incorporate CTC as a screening option.

- **Screening optical colonoscopy costs are understated** - The estimated cost of a screening optical colonoscopy in the AHRQ report (\$522.47) appears to be too low because hospital outpatient facility payments for optical colonoscopy have increased substantially since 2007. We estimate that the correct cost of a screening optical colonoscopy is \$708.07, more than one-third higher than the cost estimate used in the AHRQ report. AHRQ's estimated cost of an optical colonoscopy also excludes any payment for anesthesia, which should be considered.
- **Clarification of per-polyp vs. per-patient usage in analyses** - The report uses per-polyp, rather than per-patient, data to measure the accuracy of CTC colonography. Per-patient accuracy data are more clinically relevant than per-polyp accuracy data because the goal of colorectal cancer screening with CT colonography is correct triage of patients to optical colonoscopy for confirmation and potential biopsy / polypectomy.
- **Small polyp accuracy methodology is not transparent** – The report provides no information on how sensitivity and specificity values for 6mm-9mm polyps were derived. The sensitivity and specificity parameters for CTC that were used in the report likely understate CTC's true accuracy.
- **Extracolonic findings analyses should be expanded** - If one agrees with the AHRQ report's assumption that follow-up care for extracolonic findings is cost effective, than a penalty should be assigned to the other screening strategies because they miss opportunities for cost-effective interventions. For example, CTC can identify abdominal aortic aneurisms (AAA) whose treatment is cost-effective.² Consequently the increased costs and loss of life years lost from not identifying AAA with stool-based or endoscopic screening should be incorporated in the costs and benefits of these screening technologies.

Detailed Comments

1. When properly interpreted, the report concludes that CT Colonography (CTC) would be a highly cost-effective addition to Medicare's current colorectal cancer screening benefit.

- The report's primary analyses follow conventional health technology assessment methods by implicitly assuming that CTC can only replace existing screening technologies.
- However, evidence suggests that CTC will increase the number of beneficiaries screened because patients prefer non-invasive tests.³ The actual impact of CTC on screening cannot truly be determined until it becomes a covered benefit.
- The report also acknowledges that CTC has the potential to increase screening adherence, but its evaluation of CTC's impact on screening adherence is limited to a rudimentary and incomplete sensitivity analysis.⁴
- Because CTC is likely to increase screening adherence, it should be evaluated by comparing Medicare's current screening *program* (stool testing or endoscopic examinations) to probable Medicare screening *program scenarios* that incorporate CTC as a screening option.
- The decision errors that result from evaluating CTC using standard methods are underscored by the report's surprising conclusion that most existing CRC screening strategies are not cost effective. Specifically, 71%, 79% and 93% of screening strategies examined are not cost

effective in the MISCAN, SimCRC and CRC-SPIN simulations, respectively. Remarkably, reliance on the CRC-SPIN model would result in Medicare covering only 10-year optical colonoscopy screening, not stool testing or other endoscopic screening procedures.

- GEHC conducted a scenario-based evaluation of CTC using data from the report, and found that **every plausible scenario for adding CTC to Medicare's CRC screening benefit is cost effective at a threshold of \$50,000 per life-year gained.**
- Details of our analysis are available on request. Briefly, we first defined four screening options: No screening; stool-based screening; endoscopic screening; and CTC screening. Second, we used data from the 2005 NHI survey reporting that 43%, 12%, and 45% of patients were associated with the no screening, stool screening and endoscopic screening options, respectively.⁵ Next, we estimated costs and life-years gained (LYG) under a "base-case" Medicare screening scenario as the weighted average of LYG and costs under each option. Finally, we computed Incremental Cost Effectiveness Ratios (ICERs) for a variety of Medicare colorectal cancer screening scenarios that reflected various degrees of switching from no screening, stool-based screening or endoscopy screening to CTC screening.
- Results reported in Table 1 show that adding CTC as a screening option is cost effective (ICER ≤\$50,000) for all strategies, except those in which an extremely high percentage of patients (approximately 85%) switch from stool or endoscopic screening to CTC.

AHRQ should consider rerunning their analyses to evaluate whether adding CTC to the current screening benefit is cost-effective under the conditions described.

2. The cost of a screening optical colonoscopy appears to be understated

- The estimated cost of a screening optical colonoscopy in the AHRQ report appears to be \$522.47 too low because hospital outpatient facility payments for optical colonoscopy have increased substantially since 2007.
- We estimate that the correct cost of a screening optical colonoscopy is \$708.07, more than one-third higher than the cost estimate used in the AHRQ report.⁶
- Specifically, hospital outpatient facility payments for codes 44378, G0105 and G0121 used in the AHRQ report were \$352.9, \$334.5 and \$334.5, respectively. The corresponding 2009 national payment rates are \$593.76, \$528.10 and \$528.10, respectively. 2009 rates for other facility and professional components were somewhat higher as well.
- The AHRQ's estimated cost of an optical colonoscopy (and our own) also excludes any payment for anesthesia. AHRQ should investigate how frequently anesthesia is administered with optical colonoscopy and adjust the payment amount used in their analyses accordingly.

AHRQ should re-compute the cost of an optical colonoscopy screening examination to reflect recent changes in payment, adjust that cost as appropriate for the use of anesthesia, and repeat its analyses using the revised cost data.

3. The CTC accuracy data used in the report may be inappropriate

- The report uses per-polyp, rather than per-patient, data to measure the accuracy of CTC colonography.
- Per-patient accuracy data are more clinically relevant than per-polyp accuracy data because the goal of colorectal cancer screening with CT colonography is correct triage of patients to optical colonoscopy for confirmation and potential biopsy / polypectomy.⁷

- Whether a patient has one or many polyps is irrelevant: patients with *any* lesion reaching a certain size threshold will be referred for a complete optical colonoscopy and likely polypectomy.
- Inappropriate use of per-polyp data would underestimate the cost effectiveness of CTC because sensitivity and specificity of CTC are greater when measured on a per-patient basis.
- Per-polyp accuracy data is only reported because it increases our understanding of the technical capability of CTC; such data are important because optical colonoscopy is not a perfect reference standard, but it can frequently ignore the interdependence of data.⁸

AHRQ should repeat their analyses using per-patient CTC accuracy data, or justify why per-patient accuracy data are inappropriate.

4. The method used to derive CTC accuracy data for small (6mm-9mm) polyps is not transparent.

- Neither Pickhardt (2003)⁹ nor Johnson (2008)¹⁰ directly report CTC accuracy data for 6mm-9mm polyps; rather, they report statistics for varying polyp thresholds (e.g., ≥ 6 mm, ≥ 7 mm and so on).
- The report provides no information on how sensitivity and specificity values for 6mm-9mm polyps were derived.
- The sensitivity and specificity parameters for CTC that were used in the report appear to understate the true accuracy of CTC. For example, the report assumes an “ACRIN” per polyp sensitivity of 57% for polyps of 6-9mm, but reported per-polyp sensitivities ranged from 70% for polyps ≥ 6 mm to 82% for polyps ≥ 9 mm. The per-patient ACRIN sensitivities ranged from 78% for polyps ≥ 6 mm to 90% for polyps ≥ 9 mm.

AHRQ should explain the source of CTC accuracy data used in their analyses and revise their results accordingly.

5. The report should expand its extracolonic findings discussion

- The report states, “Although the prevalence of extracolonic findings has been reported (Levin 2008) as well as costs (Pickhardt 2008a), the long-term benefit of working up the various extracolonic findings is not well documented. *The implicit assumption that we are making by not formally incorporating these costs and benefits is that, conditional on a CT colonography examination being done, cost-effective approaches to follow-up care of extracolonic finding are being adopted* (emphasis added).”
- If the assumption that follow-up care for extracolonic findings is cost effective, then a penalty should be assigned to the other screening strategies because they miss opportunities for cost-effective interventions. For example, CTC can identify abdominal aortic aneurisms (AAA) whose treatment is cost-effective.¹¹ Consequently the increased costs and loss of life years from not identifying AAA with stool-based or endoscopic screening incorporated in the costs and benefits of these screening technologies.
- It should also be noted that Hassan (2008)¹¹ included the impact of extracolonic findings in their cost-effectiveness analysis, and concluded that, “When detection of extracolonic findings such as AAA and extracolonic cancer are considered in addition to colorectal neoplasia in our model simulation, CT colonography is a dominant screening strategy (i.e., more clinically effective and more cost-effective) over both colonoscopy and colonoscopy with 1-time ultrasonography.” The frequency, severity, cost and overall impact of extracolonic findings on the cost effectiveness of CTC, however, remain controversial.^{12, 13, 14}

Table 1. Cost-Effectiveness of Adding CT Colonography as screening option

Scenario	Screening Adherence Rates			MISCAN			Sim-CRC			CRC-SPIN		
	No Screen	Stool	Endoscopy	Cost	Life-Years Gained	ICER**	Cost	Life-Years Gained	ICER**	Cost	Life-Years Gained	ICER**
<i>Current Medicare Program (Baseline)</i>	43.0%	12.0%	45.0%	\$2,800,053	48.1	n/a	\$2,245,886	51.0	n/a	\$1,753,839	56.9	n/a
All CTC patients were previously unscreened	38.0%	12.0%	45.0%	\$2,838,787	52.2	\$9,529	\$2,262,816	55.4	\$3,883	\$1,763,633	61.8	\$1,999
All CTC patients were previously screened with stool testing	43.0%	7.0%	45.0%	\$2,839,102	48.4	\$137,819	\$2,277,156	51.7	\$45,986	\$1,785,913	57.9	\$33,180
All CTC patients were previously screened with optical colonoscopy	43.0%	12.0%	40.0%	\$2,829,204	47.8	d	\$2,272,506	50.7	d	\$1,782,465	56.5	d
90% of CTC patients previously unscreened*	38.5%	11.9%	44.6%	\$2,838,037	51.7	\$10,426	\$2,263,883	55.0	\$4,600	\$1,765,589	61.3	\$2,670
80% of CTC patients previously unscreened*	39.0%	11.8%	44.2%	\$2,837,287	51.3	\$11,559	\$2,264,950	54.5	\$5,503	\$1,767,544	60.8	\$3,513
70% of CTC patients previously unscreened*	39.5%	11.7%	43.8%	\$2,836,537	50.9	\$13,033	\$2,266,017	54.1	\$6,673	\$1,769,500	60.3	\$4,603
60% of CTC patients previously unscreened*	40.0%	11.6%	43.4%	\$2,835,787	50.5	\$15,030	\$2,267,084	53.6	\$8,251	\$1,771,456	59.8	\$6,069
50% of CTC patients previously unscreened*	40.5%	11.5%	43.0%	\$2,835,037	50.0	\$17,888	\$2,268,150	53.2	\$10,496	\$1,773,412	59.3	\$8,143
40% of CTC patients previously unscreened*	41.0%	11.4%	42.6%	\$2,834,288	49.6	\$22,319	\$2,269,217	52.7	\$13,941	\$1,775,368	58.8	\$11,304
30% of CTC patients previously unscreened*	41.5%	11.3%	42.2%	\$2,833,538	49.2	\$30,111	\$2,270,284	52.3	\$19,903	\$1,777,324	58.3	\$16,712
20% of CTC patients previously unscreened*	42.0%	11.2%	41.8%	\$2,832,788	48.8	\$47,428	\$2,271,351	51.8	\$32,727	\$1,779,279	57.8	\$28,081
10% of CTC patients previously unscreened*	42.5%	11.1%	41.4%	\$2,832,038	48.4	\$119,192	\$2,272,418	51.4	\$80,311	\$1,781,235	57.3	\$67,360

*Remaining patients drawn proportionally from other stool and optical colonoscopy screening

**Incremental Cost-Effectiveness Ratio

d=dominated

Notes:

¹ BlueCross BlueShield Technology Evaluation Center, *CT Colonography ("Virtual Colonoscopy") for Colon Cancer Screening*, accessed via web November 24, 2008. <http://www.bcbs.com/blueresources/tec/press/ct-colonography-virtual.html>

² Hassan C, Pickhardt P, Laghi A et al. Computed Tomographic Colonography to Screen for Colorectal Cancer, Extracolonic Cancer, and Aortic Aneurysm: Model Simulation With Cost-effectiveness Analysis. *Arch Intern Med* 2008 April 14;168(7):696-705.

³ "Studies examining unscreened patients for preference of a screening method find that patients fall into two groups – those that consider accuracy as the most important factor in their choice of screening modality and those that consider the invasiveness of a test as the most important factor. In a study by Schroy (2007), among currently available screening options, colonoscopy was clearly the preferred screening option (133/263; 52%), with patients citing accuracy as the most important reason for choosing colonoscopy. Importantly, remaining patients who did not choose colonoscopy still considered accuracy an important factor in their choice of a screening option, suggesting that there is a group of patients who are adverse to the invasiveness of optical colonoscopy who might be amenable to screening using CT colonography should its accuracy be deemed comparable." Source: Roberta Scherer, Amy Knudsen, and Steven D. Pearson. Final Appraisal Document: CT Colonography

For Colorectal Cancer Screening. Institute For Clinical And Economic Review. January 27, 2008. (Schroy P. C. III, Lai S., Glick J. T., Robinson P. A., Zamor P., Heeren T. C. 2007. Patient preference for colorectal cancer screening: How does stool DNA testing fare? *Amer. J. Managed Care* 13:393-400.)

⁴ Specifically, 50% of patients (500) are assumed to receive the non-CTC screening strategies, while 50% and 62.5% of patients are assumed to receive a CTC strategy. Results are reported in terms of CTC study costs needed for CTC to be on the efficient frontier, cost-neutral compared to no screening, equal to the highest ACER or equal to the colonoscopy ACER

⁵ Shapiro JA, Seeff LC, Thompson TD, Nadel MR, Klabunde CN, Vernon SW. Colorectal cancer test use from the 2005 National Health Interview Survey. *Cancer Epidemiol Biomarkers Prev.* 2008; 17(7):1623-30

⁶ Our estimate includes AHRQ's recommended 5% increase to account for colonoscopies that need to be repeated due to inadequate preparation

⁷ AH Dachman and ME Zalis *Radiology* 2004; 230:319 Quality and consistency in CT colonography and Research reporting

⁸ Halligan S, Taylor SA. CT colonography: results and limitations. *Eur J Radiol* 2007 March;61(3):400-8.

An example of the impact of using per patient or per polyp sensitivity:

"In an extreme example, imagine a study of 10 patients, 9 of whom have a single polyp each but where the tenth patient has 10 polyps (i.e. the study population has 19 polyps in total). That single patient will contribute disproportionately to a per-polyp analysis. If the single polyp in all other patients is detected but none are detected in the tenth patient (because of poor bowel preparation or distension for example), then sensitivity will be 0.47 (i.e. 9 of 19 polyps detected). Per-patient analysis of the same data will yield very different results, a sensitivity of 0.9 (i.e. 9 of 10 patients correctly categorised). It is important to recognise that when a single polyp is well-depicted in a patient, other polyps in the same patient are also likely to be well-depicted because they are all subject to similar circumstances of bowel preparation, distension, colonic anatomy, compliance with breathing instructions, etc. The converse is also true. This interdependence of data (also known as 'clustering' or 'correlation') is frequently ignored."

⁹ Pickhardt PJ., Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med* 2003;349:2191-2200.

¹⁰ Johnson CD, Chen M-H, Toledano AY, et al. Accuracy of CT colonography for detection of large adenomas and cancers. *N Engl J Med* 2008;359:1207-17.

¹¹ Hassan C, Pickhardt P, Laghi A et al. Computed Tomographic Colonography to Screen for Colorectal Cancer, Extracolonic Cancer, and Aortic Aneurysm: Model Simulation With Cost-effectiveness Analysis. *Arch Intern Med* 2008 April 14;168(7):696-705.

¹² Fletcher RH, Pignone M. Extracolonic findings with computed tomographic colonography: asset or liability? *Arch Intern Med* 2008 April 14;168(7):685-6.

¹³ Pickhardt PJ, Hanson ME, Vanness DJ et al. Unsuspected extracolonic findings at screening CT colonography: clinical and economic impact. *Radiology* 2008 October;249(1):151-9.

¹⁴ Flicker MS, Tsoukas AT, Hazra A, Dachman AH. Economic impact of extracolonic findings at computed tomographic colonography. *J Comput Assist Tomogr* 2008 July;32(4):497-503.

GEHC very much appreciates this opportunity to comment. We look forward to working with AHRQ to help enable high-quality, clinically effective healthcare services that save lives.

Sincerely,

A handwritten signature in black ink that reads "Hugh Zettel". The signature is written in a cursive, flowing style.

Hugh Zettel
GE Healthcare
Strategic Reimbursement Executive

cc: Steve Phurrough, M.D.,
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